

INVITED SPEAKER PRESENTATION

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Immunopathology and dexamethasone therapy in a new model for malaria-associated acute respiratory distress syndrome

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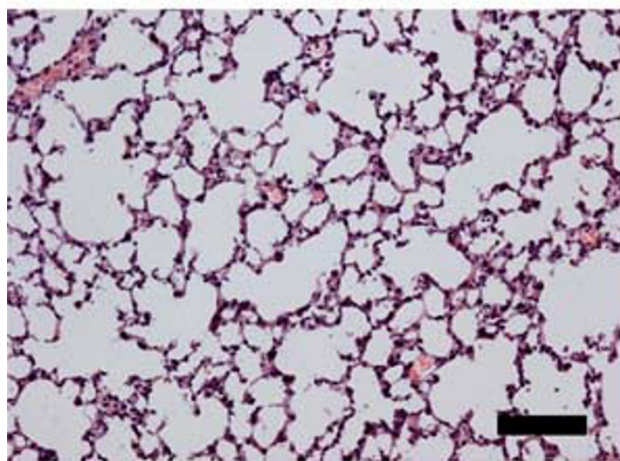
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Malaria infection is often complicated by malaria-associated acute respiratory distress syndrome (MA-ARDS), characterized by pulmonary edema and hemorrhages. No efficient treatments are available for MA-ARDS and its pathogenesis remains poorly understood. To develop a new animal model for MA-ARDS, mice were infected with *Plasmodium berghei* NK65, and the development of MA-ARDS was characterized by increased lung weight, edema, leukocyte infiltration and hemorrhages (Figure 1). The pulmonary expression of several cytokines and chemokines was increased to a higher level than in mice

infected with *P. chabaudi* AS, which does not cause MA-ARDS. By depletion experiments, CD8⁺ T lymphocytes were shown to be pathogenic. High doses of dexamethasone blocked MA-ARDS, even when administered after appearance of the complication, and reduced pulmonary leukocyte accumulation.

We developed a novel model of MA-ARDS with many similarities to human MA-ARDS and without cerebral complications. This contrasts with the more classical model with *P. berghei* ANKA, characterized by fulminant cerebral malaria. Hence, infection with *P. berghei* NK65

Uninfected control



***P. berghei* NK65 infected**

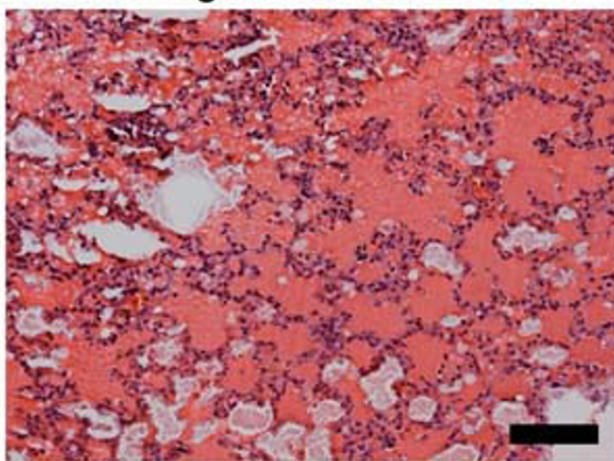


Figure 1 Histopathology of *P. berghei* NK65-induced MA-ARDS. Frozen sections of lungs of mice infected for 10 days with *P. berghei* NK65 or control mice were stained with H&E. The black bar corresponds with 100 μ m.

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generates a broader time window to study the pathogenesis and to evaluate candidate treatments. The finding that high doses of dexamethasone cured MA-ARDS suggests that it might be more effective against MA-ARDS than it was in the clinical trials for cerebral malaria.

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